Allergy Abstracts

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Asthma and Hay Fever

Volumetric and Gravity Slide Tests for Air-Borne Ragweed and Oak Pollens at Columbus, Ohio. Gilbert, G. E.: Ohio J. Sc. **50**: 60, 1950.

The daily atmospheric ragweed pollen concentration at Columus, Ohio, during the first half of September, 1948, was determined simultaneously by the standard gravity slide technique and by an efficient volumetric sampling procedure. The average daily ratio of the pollen counts obtained by each method was 4.57. Durham's conversion factor of 3.87 for giant ragweed, when corrected for the smaller size of pollens in the Ohio area, was 4.68 and compared favorably with the author's experimentally determined factor. It is suggested that the factor 4.57 be used in converting gravity slide counts to volumetric counts during years when tall ragweed pollen is predominate. When short ragweed pollen is the dominant type, Durham's conversion factor of 3.6, corrected for local differences in the size of ragweed pollen, should be used.

Similar comparative data was obtained by volumetric and gravity tests during six days of the 1949 oak pollen season. The average daily ratio of the counts obtained by the two methods was 1.3, which again closely approximated Durham's calculated conversion factor for oak pollen.

These studies lend support to the accuracy of Durham's calculations for the determination of conversion factors for various hay fever pollens by reference to their relative rates of fall as compared to that of short ragweed. B. S.

Mold Fungi in the Etiology of Respiratory Allergic Diseases. XI. Phytopathogenic Fungi in Aerobiological Populations. Morrow, M. B., and Thiers, H. D. Ann. Allergy **7**: 592, 1949.

The role of phytopathogens as allergenic material in an air population was studied. An attempt was made to determine whether host symptoms were an

index of air-borne spores, whether air-borne spores were carried any distance, and whether spore incidence was seasonal and corresponded to the seasonal incidence of the host's infection. The smuts of Johnson and Bermuda grass, the rusts of Johnson grass and Dichondra, and the powdery mildews of crape myrtle, Evonymus, and wild China were selected for study. Samples of air population were obtained on adhesive slides exposed within thirty feet of infected plants. Dissemination of spores was studied on slides placed at greater distances. Spores of the following six pathogens were air borne locally: the smuts, Johnson grass rust, and the powdery mildews. Of these, only Johnson grass smut and crape myrtle powdery mildew were recovered at a distance. There seemed to be a seasonal variation in the presence of the smuts and this variation could be correlated with host symptomatology. The fact that Johnson grass smut was recovered from the air after host symptoms had disappeared may have some clinical significance. W.

Mold Fungi in the Etiology of Respiratory Allergic Diseases. XII. Further Studies With Mold Extracts. Prince, H. E., Arbesman, C. E., Sellers, E. D., Petit, P. T., Brown, E. A., and Morrow, M. B.: Ann. Allergy **7**: 597, 1949.

Cross-neutralization studies were made on the sera of fourteen mold-sensitive patients with acetone-precipitated glycerol-saline extracts of Alternaria, Hormodendrum, Spondylocladium, Helminthosporium, Curvularia, and Nigrospora. In in vivo neutralization studies, passive transfer sites were prepared with 0.08 to 0.10 ml. of serum and were tested two days later with Alternaria 1:1,000. After twenty-four hours, one site was tested with homologous mold extract and, if the reaction was negative, the other sites were tested with heterologous molds. This procedure was repeated with Hormodendrum and the other molds. In in vitro neutralization experiments, sites were prepared with mixtures of equal amounts of serum and mold extract in 1:1,000 dilution. After forty-eight hours, the sites were tested with 0.05 ml. of each of the respective mold extracts in dilutions of 1:10,000. Shortly thereafter, these sites were retested with the same molds in 1:1,000 dilution. Each mold was tested in succession. In ten of the sera studied, Alternaria exhausted the reagins for all other molds. "In general, the antibody exhausting power of any particular mold seemed unpredictable except for the fact that those molds giving large transfer reactions on the initial testing in the in-vivo neutralizations seemed to neutralize more reagins for other molds, and they in turn seemed more difficult to be neutralized." All the sera differed in reaginic content. The dematiaceous molds studied seemed to contain group antigens as well as generic or possibly specific antigens. In the light of these findings, the rationale of using Alternaria alone in the treatment of patients showing reactions to other molds of the dermatiaceous group must be questioned. W.

Mold Fungi in the Etiology of Respiratory Allergic Diseases. XIII. The Use of a Concentrated Extract in the Treatment of Mold-Sensitive Patients. Figley, K. D., and Rawling, F. A.: Ann. Allergy **7**: 610, 1949.

The potency of an acetone-precipitated glycerol-saline extract of Alternaria (Alternaria 33) was compared with commercial extracts by the scratch technique in 200 mold- and pollen-sensitive patients. It was found that Alternaria 33 in dilutions of 1:200 gave skin reactions comparable to those obtained with concentrated commercial extracts. Among the patients tested, only 15 showed pure Alternaria sensitivity. Treatment was begun with dilutions of 1:200,000 and rarely exceeded dilutions of 1:2,000. Constitutional reactions were some-

times encountered. It was concluded that Alternaria 33 was a nonirritating, uniformly potent extract that afforded satisfactory results in the treatment of Alternaria-sensitive patients. W.

Allergic Examination of Bakers and Millers. Castberg, T., and Sorenson, C. M.: Acta allergologica **1**: 283, 1948.

One hundred thirty bakers and millers employed in five different bakeries in Copenhagen were questioned for the presence of allergic symptoms. Forty-two of the 130 reported nondisabling symptoms, 14 of the 42 complained of asthma, 13 of vasomotor rhinitis, 8 of eczema, 6 of urticaria, and 1 of hemicrania. Ninety-two of the 130 were tested by the intracutaneous technique with various flours, flour-improving substances, and pollens. Thirty-nine (41.9 per cent) showed positive reactions to flours, but only 26 of these had allergic symptoms. The majority of the bakers were sensitive to rye flour, which is the flour used extensively in Denmark. H.

Blood Examination in Hay Fever Patients During Acute Allergic Shock. Castberg, T., and Schwartz, M.: Acta allergologica **1**: 272, 1948.

The bloods of five hay fever patients were examined at the time when they developed constitutional reactions following pollen injections. Symptoms during the reactions consisted of erythema, pruritus, urticaria, nasal symptoms, and asthma. Blood samples were taken from three to six minutes after the onset of the constitutional reactions and every fifteen minutes thereafter for one hour.

A distinct fall in blood sugar followed by an incipient secondary rise was noted. A definite, transient leucopenia with a fall of about 1000/c.mm. was observed. The hemoglobin, coagulation time, and thrombocyte count were normal throughout the shock period. Serum bicarbonates, serum chlorides, and fibrinogen values were unchanged. The sedimentation rate was not altered. There was no change in the blood eosinophile count. A slight drop in blood pressure was noted at the onset of the constitutional symptoms in one patient. H.

Bronchiectasis: A Study of the Segmental Distribution of the Pathologic Lesions. Moore, J. R., Kobernick, S. D., and Wiglesworth, F. W.: Surg., Gynec. & Obst. **89**: 145, 1949.

In seven cases of early bronchiectasis in children treated surgically, the pathologic findings were not entirely consistent with the bronchographic studies. Detailed microscopic examination showed definite inflammatory lesions and sometimes advanced lesions in segments which, bronchographically and on gross examination, appeared unaffected. Occasionally, lesions were found to be minimal where bronchography showed moderate involvement. When the disease was present to such a degree as to be visible bronchographically, the adjacent segments were usually found to be involved, though to a lesser degree.

Caution, therefore, must be exercised in evaluating the extent of bronchiectatic lesions prior to surgery. J. S.

Observations on the Clinical Use of Visammin (Khellin). Rosenman, R. H., Fishman, A. P., Kaplan, S. R., Levin, H. G., and Katz, L. N.: J. A. M. A. **143**: 160, 1950.

Visammin (khellin), a crystalline compound obtained from the plant, Ammi visnaga Lam, produces vasodilation and relaxes smooth muscle in animals. The drug was administered to a series of patients suffering from angina pectoris, chronic cor pulmonale, and acute bronchial asthma. In angina pectoris and

in cor pulmonale, the results were excellent. The patients experienced marked relief of dyspnea, wheezing, and other respiratory distress. There was a decrease in cyanosis, an increase in exercise tolerance, and an increased sense of well-being. Among twenty-one cases of bronchial asthma treated with the drug, excellent but transitory relief was obtained in nine patients and moderate relief in three. Side effects, such as nausea, vomiting, and skin eruptions, were observed in a high percentage of the patients. F.

Dermatology

The McClure-Aldrich Test in Dermatology With Special Reference to the Dermatoses. Canisares, O., Combes, F. C., Simnangco, S., and Kaufman, J.: J. Invest. Dermat. **13**: 325, 1949.

Intracutaneous tests with 0.1 c.c. of a 0.8 per cent solution of sodium chloride were performed on the flexor aspect of the forearms and the extensor aspect of the thighs of 29 patients with bullous dermatoses and 86 patients with various other types of dermatoses. The normal disappearance time of the wheal (McClure-Aldrich test) was 30 minutes or longer. It was consistently rapid in cases of exfoliative dermatitis, urticaria, dermatitis hypostatica, and disseminated lupus erythematosus. The disappearance time was rapid in apparently normal areas within 5.0 cm. of eczematous lesions. In the bullous dermatoses, there was a rapid disappearance time. In pemphigus, vulgaris, it became rapid several weeks after the onset of the disease and remained so regardless of variations of the clinical picture. In bullous erythema multiforme and dermatitis herpetiformis, the disappearance time was rapid during the exacerbations and later returned to normal. The authors believe that the intracutaneous saline test is a measure of the degree of local edema.

I. GLAZER.

The Serum Proteins in Diseases of Connective Tissue. An Electrophoretic Study. Walker, S. A., and Benditt, E. P.: J. Invest. Dermat. **14**: 113, 1950.

In acute disseminated, subacute, and chronic discoid lupus erythematosus, in diffuse and circumscribed scleroderma, and in rheumatic fever, electrophoretic study showed a decrease in serum albumin and an increase in serum gamma globulin. In dermatomyositis, there was no statistically significant increase in gamma globulin concentration, the only change being a decrease in albumin and in total protein. The rise in gamma globulin was suggestive of antibody production and offered presumptive evidence for the association of lupus erythematosus, scleroderma, and rheumatic fever with antigen-antibody reactions. I. GLAZER.

Exfoliative Dermatitis Due to Penicillin and Streptomycin. Huber, T. E.: Mil. Surgeon **105**: 4, 1949.

A debilitated 67-year-old patient with a previous history of recurrent attacks of epidermophytosis of the feet was hospitalized because of severe paroxysmal coughing and breathlessness due to chronic bronchiectasis and emphysema. He was started on penicillin therapy and after the third injection within a 24-hour period, he developed a rapidly spreading rash. Generalized exfoliation followed. Three weeks later, he was given streptomycin aerosol and after 4 days of therapy he developed a skin rash in the same area where the previous one had occurred. This rash faded shortly after the streptomycin was discontinued. Skin tests showed a negative reaction to penicillin, a slightly positive reaction to streptomycin, and a 3 plus reaction to trichophyton. Apparently there is some relationship between fungus infections and reactions to the antibiotics. F.

Dermatitis Medicamentosa Due to Undecylenic Acid. Nelson, L. M.: J. Invest. Dermat. **14**: 75, 1950.

A patient who was receiving 6.0 Gm. of undecylenic acid daily for treatment of a neurodermatitis developed an erythematous rash on his face followed by an exudative dermatitis of the elbows, hands, and chin. On stopping the drugs, the lesions quickly disappeared. Within twenty-four hours following readministration, the patient developed an erythema of the areas previously involved by the exudative dermatitis. An empty capsule did not produce a flare-up and a patch test with Desenex ointment, which contains both zinc undecylenate and undecylenic acid, was negative. R. WISEMAN.

Sensitization to Antistine. Mosko, M. M., and Peterson, W. L.: J. Invest. Dermat. **14**: 1, 1950.

A 53-year-old woman with photophobia and diplopia associated with erythema, edema, and itching of the eyelids was given Antistine eye drops. The itching and edema disappeared in a few days. The same symptoms recurred again two months later and also involved the skin of the upper and lower lids bilaterally. Antistine drops were instilled again but this time caused exacerbation of all the symptoms. A demarcated contact type dermatitis was noted on the lower forehead, eyelids, cheek, and upper lip. All medications were discontinued and within a few days there was a marked improvement of the lesions. A patch test with Antistine was strongly positive in fourteen hours and caused a flare-up of the original dermatitis. Intracutaneous tests with Antistine and other antihistaminics produced no immediate reactions. However, the intracutaneous test with Antistine yielded a positive tuberculin-like reaction in forty-eight hours. Passive transfer studies with the patient's serum were negative. When the patient was tested with Antistine crystals which had been incubated with her serum for twenty-four hours, she showed a negative immediate reaction but a positive tuberculin-like reaction.

I. GLAZER.

Otorhinology and Ophthalmology

Experimental Studies on Headache: Pain Originating in Nasal and Paranasal Structures. McAuliffe, G. W., Mueller, S. C., and Wolff, H. G.: New York State J. Med. **50**: 113, 1950.

The sensitivity of various parts of the nose and paranasal sinuses was evaluated by means of a faradic stimulus. Patients experienced least pain when the stimulus was applied to the nasal septum or to the linings of the frontal or maxillary sinuses. The more sensitive nasal structures, in increasing order, were the turbinates, nasofrontal duct, and the ostium. The character of the pain was diffuse, sustained, deep, and nonpulsatile. There was associated lacrimation, photophobia, erythema, and hyperalgesia. The induced pain was referred mainly to the areas of the head supplied by the second division of the fifth cranial nerve and, to a lesser extent, to those supplied by the first division of that nerve. Pain in the back of the head or neck resulted from the secondary effects of prolonged contraction of the cervical and scalp muscles. The stimulation of several different sites resulted in pain referred to the same area. When the fifth cranial sensory nerve root was sectioned, the mucosa of the nose and paranasal structures became insensitive in most cases. The induced pain outlasted the period of stimulation. It is concluded that inflammation and engorgement of the turbinates, ostia, nasofrontal

ducts, and superior nasal spaces are responsible for most of the pain resulting from nasal or paranasal sinus disease. If zygomatic, frontal, temporal, or vertex headaches are not alleviated by shrinking or anesthetization of the nasal structures, they are, in all probability, not due to disease of the nasal or paranasal structures. B. S.

Sinusitis Due to Bacterial Allergy: Identified by Tissue Culture and Treated by Specific Desensitization. Blatt, H., and Nantz, F. A.: Ohio State M. J. **46**: 319, 1950.

Chronic sinusitis may be due to the presence of specific bacterial sensitivity. It is possible to determine the offending organism by means of a series of tissue culture tests. The patient's blood is citrated and a suspension of the white cells is made in Ringer's solution. One drop of the cell suspension, one drop of a stock bacterial filtrate, and one drop of undiluted thrombin are mixed on an ordinary glass slide and incubated for eighteen hours. Tests are made with about one hundred stock filtrates and are usually repeated on two subsequent occasions for corroboration. If hypersensitivity to an organism exists, the leucocytes become necrotic, crenated, and stippled when mixed with the specific filtrate. Patients are treated with the filtrates to which they have shown positive reactions. Dosage must be given cautiously as systemic reactions are easily provoked. Five typical cases, in which routine treatment was unsuccessful, experienced excellent results when treated with bacterial filtrates. F.

Miscellaneous Allergies

The Cellular Transfer of Cutaneous Hypersensitivity to Tuberculin in Man. Lawrence, H. S.: Proc. Soc. Exper. Biol. & Med. **71**: 516, 1949.

Fibrinogen (Fraction I) was added to heparinized sterile venous blood from tuberculin-positive normal individuals. After one hour at 37° C., the supernatant fluid containing most of the leukocytes was removed and centrifuged. The viable leukocytes were resuspended in Tyrode's solution or in serum from tuberculin-negative individuals and were injected intracutaneously into tuberculin-negative recipients. These sites and distant control sites were tested intracutaneously with tuberculin after 18, 24, or 48 hours. The reactions were read at 15 and 30 minutes and again after 24, 48, 72, and 96 hours. Sites prepared on tuberculin-negative recipients with their own leukocytes or with leukocytes of other tuberculin-negative individuals or with the serum or the erythrocytes of tuberculin-positive donors failed to react to tuberculin. Sites sensitized with leukocytes from tuberculin-positive donors yielded positive reactions with tuberculin within 48 hours. Their intensity was directly proportional to the amount of leukocytes which had been injected and the degree of tuberculin hypersensitivity of the donor. The induced cutaneous tuberculin hypersensitivity spontaneously reverted to a tuberculin-negative state after a period varying from 4 days to 3 months. I. GLAZER.

Generalized Insulin Allergy. Stone, H. H., Frankel, J. J., and Baker, L. A.: J. Clin. Endocrinol. **9**: 895, 1949.

This is a report of two patients with diabetes mellitus who developed generalized allergic manifestations following the administration of insulin. Both patients were successfully desensitized by the repeated injection of small doses of insulin and eventually tolerated a daily maintenance dose. One of the patients was eventually controlled by diet alone, and insulin was discontinued. However, when glycosuria reappeared and insulin therapy was started again,

a generalized urticaria resulted. With the aid of Pyribenzamine he was again successfully desensitized to protamine zinc insulin. In sensitive patients, the authors prefer to rely upon desensitization to insulin rather than upon dietary control. They point out the necessity for continuous insulin administration to prevent the lapse of the desensitized state. I. GLAZER.

Mechanism of Cutaneous Reactions to Insulin. Paley, R. G.: Lancet **257**: 1216, 1949.

The incidence of local reactions to insulin among 147 patients attending a diabetic clinic was 55.8 per cent. Ninety-one per cent of the reactions were of the immediate type. Intracutaneous tests were performed on these patients with soluble and protamine zinc insulin, water and buffer solutions with an adjusted pH and salmine sulfate solution. Most of the patients showed larger reactions to the insulin solutions than to the other test solutions. Intracutaneous tests made with soluble insulin were compared with those made with a solution of insulin recrystallized 6 times. It was found that recrystallized insulin produced smaller reactions. The use of recrystallized insulin also diminished the incidence of local reactions. Since spontaneous loss of local reactions occurred in about 30 per cent of this series, it is suggested that recrystallized insulin be administered where severe local reactions occur. B. S.

Allergic Meningitis and Chronic Erythema Migrans Afzelii After Bite by Ixodes Reduvius. Dalsgaard-Nielsen, T., and Kierkegaard, A.: Acta allergologica **1**: 388, 1948.

A 35-year-old woman developed a marked local reaction at the site of a tick bite. Three weeks later, an erythematous, slightly edematous ring developed at the same site and gradually spread distally on the extremity and up the trunk to the breast. A slight elevation of temperature accompained the erythema migrans. Two and one-half months after the bite, the patient developed a leucocytic meningitis with radicular symptoms. The radiculitis lasted for five and one-half months. Culture and virus studies indicated that the meningitis was not infectious. Cutaneous testing with the tick extract yielded positive reactions. Control tests were negative. The reactions were passively transferred. Similar cases reported in the literature are reviewed. H.

Cutaneous Reactions to Tobacco Antigen in Allergic and Nonallergic Children. Lima, A. D., and Racha, G.: Ann. Allergy **7**: 528, 1949.

The results of intracutaneous tests made with tobacco extracts were compared in 200 atopic and 200 nonatopic children. The incidence of positive reactions in the atopic group was 17.5 per cent as compared to 7.5 per cent among the controls. The highest incidence of positive reactions (30 per cent) was observed in 50 atopic children whose mothers smoked during gestation and lactation. Reagins were demonstrated by the passive transfer technique in 40 per cent of the positive reactors of both groups. W.

Anaphylactic Reaction to Intravenous Procaine. Schuff, L. F., and Schuff, L. J.: Anesthesiology **10**: 753, 1949.

A mild chill and dyspnea developed after the thirteenth intravenous injection of procaine (1 Gm. in 500 c.c. isotonic saline) administered for the relief of pain in arteriosclerosis. Three days after the fourteenth injection, severe dyspnea, wheezing respirations, and vasomotor collapse occurred. These symp-

toms were relieved by the use of epinephrine and antihistaminic drugs. An intracutaneous test with 1 per cent procaine, performed five days later, was negative. One month later, an attempt was made to resume procaine therapy. A similar reaction occurred. No further procaine injections were given. H.

Anaphylaxis

A Quantitative Study of the Arthus Phenomenon Induced Passively in the Guinea Pig. Benacerraf, B., and Kabat, E. A.: J. Immunol. **64**: 1, 1950.

Arthus reactions of graded severity were produced passively in guinea pigs with known amounts of antibody injected intravenously and of antigen injected intracutaneously. Complications due to anaphylaxis were eliminated by the proper control of dosage and of the time interval between sensitization and shock. Rabbit and guinea pig antiovalbumin serum and rabbit antipneumococcus type III serum, when injected intravenously, were equally able, on a weight basis, to prepare guinea pigs for Arthus reactions. The severity of the reaction was the same when the antigen was injected at once or as late as twenty-four hours after the intravenous sensitization, indicating that no latent period was necessary in the passive Arthus reaction. The residual passive anaphylactic sensitization of the animals was dependent solely upon the proportion of antigen and antibody used in eliciting the Arthus reaction and not upon its severity. When guinea pigs were sensitized intravenously with a given amount of antiovalbumin and were injected intracutaneously at four sites with large amounts of antigen, the severity of the Arthus reactions were not maximal for that amount of antigen, indicating that the excess antigen at each site was competing for the limited amount of circulating antibody. When the amount of antigen at each site was decreased, the reactions observed at the four sites were as severe as those obtained when a single site received all of the antigen. Similar phenomena were demonstrated with the reverse Arthus reaction, when the animal was injected with ovalbumin intravenously thirty minutes before the intracutaneous dose of antibody. When guinea pigs were sensitized intracutaneously with known amounts of antiovalbumin sera, equally severe Arthus reactions were elicited twenty-four hours later whether the antigen was injected at the same site or at any other site. This confirmed the importance of the role of circulating antibody in the Arthus reaction. Much more antibody was required to cause a minimal reaction in the direct Arthus reaction, using intravenous sensitization, than for a reverse reaction.

Equivalent weights of nonprecipitable ("univalent") rabbit antiovalbumin were unable to cause Arthus reactions comparable in severity to those produced by the antibody in whole serum. Concentrated horse antipneumococcus type I serum was able to induce Arthus reactions but did not confer passive anaphylactic sensitivity in guinea pigs.

It is suggested that the Arthus reaction should not be considered a form of local anaphylaxis. In contrast to anaphylaxis, which is mediated by a fixed antibody, the Arthus reaction is caused by a circulating one and does not require a latent period in passive sensitization.

Observations on the vessels of the skin and subcutaneous tissue of the site of an Arthus reaction revealed vasospasm, fragmentation of the vessels, and eventually shutting off of the blood supply to the area. The Arthus phenomenon is considered to be fundamentally an inflammatory reaction of the tissue with the production of hemorrhage and necrosis caused by injury to small blood vessels as a result of the reaction of circulating precipitin and locally introduced antigen. I. GLAZER.

A Study of the Effect of Adrenocorticotropic Hormone (ACTH) Upon the Experimental Cardiovascular Lesions Produced by Anaphylactic Hypersensitivity. Berthrong, M., Rich, A. R., and Griffith, P. C.: Bull. Johns Hopkins Hosp. **86**: 131, 1950.

Forty rabbits were given a single intravenous injection of 10 c.c. of sterile horse serum per kilo of body weight. Beginning on the same day, one-half were treated intramuscularly with large doses (5 mg.) of ACTH, every six hours for a week and then with smaller daily doses until they were killed. The remainder served as controls. On the twelfth day, all animals showed positive reactions to intracutaneous tests with 0.1 c.c. of horse serum. On the fifteenth to eighteenth day, when they were killed, the sera of the ACTH-treated and of the control animals contained precipitins for horse serum, the titer of the untreated ones being slightly higher. The ACTH, therefore, neither prevented the development of hypersensitivity nor abolished the capacity of the sensitized tissue to react to the antigen. Histologic sections made of the organs showed well-marked vascular or cardiac lesions, or both, in 18 of 20 untreated controls, whereas such lesions were found in only 5 of 20 animals treated with ACTH. This suggested that ACTH exerted an inhibitory effect upon the development of cardiovascular lesions of hypersensitivity. I. GLAZER.

Tuberculin Reaction. IV. Failure of Pyribenzamine To Protect Against Systemic Tuberculin Shock. Weiser, R. S., Evans, E., and St. Vincent, L.: Proc. Soc. Exper. Biol. & Med. **73**: 303, 1950.

Large guinea pigs, weighing 600 to 1000 grams were injected intraperitoneally with a young culture of B.C.G. Twenty-four days later, the animals showed a strong reaction to an intracutaneous injection of 1:100 O.T. On the thirty-fourth day after inoculation, an intraperitoneal shock dose of 5 or 10 ml. of 1:5 O.T. was given. Some of the guinea pigs received subcutaneous injections of from 5 to 14 mg. Pyribenzamine per kg. in divided doses starting three hours before and ending two hours after the shocking dose. All the animals, whether treated or untreated with Pyribenzamine, developed typical severe systemic tuberculin shock in from three to four hours and manifested no significant differences in survival time. It is concluded that histamine or histamine-like substances do not play a significant role in tuberculin shock. I. GLAZER.

On the Toxic and Allergic Manifestations Caused by the Tissues and Fluids of Ascaris. II. Effect of Different Chemical Fractions on Worm-Free, Infected, and Sensitized Guinea Pigs. Sprent, J. F. A.: J. Infect. Dis. **86**: 146, 1950.

Ascaris body fluid and extracts prepared from various tissues of the worm contain a substance capable of causing anaphylactoid reactions when introduced intravenously into worm-free guinea pigs. This anaphylactoid-producing substance is presumably associated with protein, since it is almost completely removed by protein precipitants, by boiling, and by complete digestion with pepsin. The severity of the reaction and the rapidity of death seem to depend upon the amount of material injected. Typical anaphylactic shock could be produced with small amounts of Ascaris extract in animals experimentally sensitized or infected with larvae. These reactions occurred even after the removal of protein from the extracts. Cross sensitivity was demonstrated by the fact that shock could also be produced with Ascaris extracts in animals infected with various other nematodes. It was concluded that, although the protein fraction plays a role in producing the anaphylactic reaction, other substances, such as polysaccharides, appear to be of equal importance. F.

Pharmacology, Physiology, and Pathology

Biological and Technical Factors in the Demonstration of Antibody Production by Lymphatic Tissue. Harris, T. N., and Harris, S.: J. Immunol. **64**: 45, 1950.

The authors present experiments demonstrating the capacity of the lymph nodes to form antibodies.

Two groups of rabbits were injected in the hind leg with Shigella organisms, one series receiving a much larger dose than the other. Extracts made from popliteal nodes draining the injected leg were compared with nodal extractions derived from the other hind leg. When only a small quantity of antigen was introduced, there was a striking difference between the antibody titers of the contralateral lymph nodes. This was not observed when large amounts of Shigella were used. Eight animals in the series which were also injected subcutaneously with washed sheep erythrocytes showed equal hemolysin titers in extracts of the popliteal nodes from both legs.

Lymph was collected from the draining channels of the nodes producing high titers. The lymphocytes were separated from the fluid and treated by numerous washings and repeated freezings and thawings in order to produce fragmentation. Following vigorous handling, the cell antibody titer was markedly diminished to a point even lower than that of the lymph plasma. However, even with minimal washing of the cells, there was a lowering of the cell antibody titer. The authors suggest that the ease with which lymphocytes release antibodies may explain why lymph fluid in the central portion of the body contains cells with relatively low titers. R. WISEMAN.

Lesions of Hypersensitivity Induced in Rabbits by Massive Injections of Horse Serum. More, R. H., and McLeon, C. R.: Am. J. Path. **25**: 413, 1949.

Seventy-seven rabbits were sensitized with horse serum by one or more intravenous injections of 10 c.c. of horse serum per kilogram of body weight. The animals were autopsied ten days after the last injection. Sixty per cent showed an arteritis similar to human periarteritis nodosa. Inflammatory lesions of the heart valves were found in 20 per cent of the treated animals. Similar cardiac lesions, however, were present in 80 per cent of the controls. The only lesion resembling rheumatic carditis occurred in one of the controls. Aschoff-like lesions were not encountered. These findings failed to confirm the studies of Rich and Gregory who produced lesions similar to human rheumatic carditis in rabbits by injecting large doses of horse serum intravenously. J. S.

Adsorption, Distribution and Excretion of Tripelennamine (Pyribenzamine). Way, E. L., and Dailey, R. E.: Proc. Soc. Exper. Biol. & Med. **73**: 423, 1950.

A modification of the Brodie methyl orange technique was used for estimation of tripelennamine in tissues. Within four hours after oral administration of 100 mg./kg. of tripelennamine to rats, the drug had almost completely disappeared from the gastrointestinal tract. When the animals were sacrificed immediately after the compound was administered and the entire gastrointestinal tract was incubated for two hours, there was no alteration in the tripelennamine concentration.

After intraperitoneal administration of 50 mg./kg. of tripelennamine, the compound disappeared rapidly from the blood. Appreciable amounts were concentrated in the brain, kidneys, spleen, liver, heart, and especially the lungs. The drug was not detectable in tissues twenty-four hours after its repeated ad-

ministration for several days. Oral administration resulted in elevated levels in the liver. Studies made on guinea pigs gave a similar distribution pattern. In four human beings, after 50 to 100 mg. tripelennamine orally, less than 1 per cent was recoverable in the urine after from fifteen to twenty-four hours. In rats which were give 50 mg./kg. of the drug intraperitoneally, less than 2 per cent of it was found in the urine in twenty-four hours. After aerobic incubation of tripelennamine with liver slices for two hours, only 10 per cent of the compound was recovered. Intraperitoneal administration of 40 mg./kg. of tripelennamine caused severe convulsions in partially hepatectomized rats but not in laparotomized ones. The authors conclude that the drug is almost completely metabolized in the body and most actively in the liver. I. GLAZER.

Investigations of the Functions of the Suprarenal Cortex in Allergic Diseases. Eriksson-Lihr, Z., Forssell, P., Pettay, O., and Rusk, I.: Acta allergologica 2: 299, 1949.

Adrenal cortical activity was studied in patients with asthma, allergic eczema, allergic rhinitis, and urticaria. In evaluating the desoxycorticosterones (saltwater factor), the first part of the Robinson-Power-Kepler test was performed on sixty-four allergic patients and found to be positive in twenty-three (35 per cent). The second part of the Kepler test was positive in only seven (10.9 per cent). These seven patients gave a history of having had allergic disturbances for from 4 to 21 years. Sodium, potassium, and chloride determinations were made in twenty-three cases. Seven of these showed low values for chlorides and sodium. In ten patients with bronchial asthma, the potassium values were increased. Only three asthmatics showed both low sodium and high potassium values.

The presence of glucosteroid (carbohydrate metabolism) in allergics was determined by means of the double dextrose tolerance test, the insulin tolerance test, and the adrenalin tolerance test. Most of the thirty-five allergic patients in whom the double glucose tolerance test was performed showed a marked initial rise indicating a normal resorption of sugar from the intestinal tract. The insulin tolerance test was performed on twenty allergic patients. Fourteen patients reacted with severe symptoms of hypoglycemia, indicating a decreased tolerance to hypoglycemia, which probably could be attributed to decreased corticosteroid excretion. A diminution in the capacity of adrenalin to raise the blood sugar level was noted in eight of ten cases.

Blood counts performed in two hundred twenty cases of bronchial asthma, allergic eczema, and allergic rhinitis with normal sedimentation rates revealed an abnormal increase in the eosinophiles and the lymphocytes.

The determination of the 17-ketosteroids in twenty-four allergic patients revealed low values in six cases. H.

Mechanism of the Acute Lethal Effect of Epinephrine in Rats. Nickerson, M., Berghout, J., and Hammerstrom, R. N.: Am. J. Physiol. **160**: 479, 1950.

In rats, death caused by intraperitoneally injected epinephrine has been shown to be the result of respiratory failure. The accumulation of epinephrine or "epinephrine-like" chromogens in the myocardium is not causally related to such deaths. This was demonstrated by experiments which showed that rats could be protected against lethal doses of epinephrine either by artificial respiration or by systemic arterial pressure stabilization when myocardial epinephrine concentrations were at a high level. Fatal pulmonary edema occurs in rabbits and guinea pigs when large doses of epinephrine are administered. This, however, is not the mechanism of death in the rat or mouse. The exact manner in

which epinephrine induces respiratory arrest is not completely clear, but it is likely that the rise in arterial pressure induced by the drug is an important etiologic factor. F.

A Study on the Treatment of the Common Cold With an Antihistaminic Drug. Shaw, C. R., and Wightman, H. B.: New York State J. Med. **50**: 1109, 1950.

Students with typical symptoms of a common cold, which had been present for forty-eight hours or less, were employed in this study. Each patient was given tablets to take every four hours and was instructed to return every day for three days. Most of the subjects took the medication for three days. Of the 443 subjects observed for the entire four days, 215 received a placebo, and 228 received 50 mg. tablets of the antihistaminic drug, 2-phenylbenzylaminomethylimidazoline hydrochloride. Fifty per cent of those who had received the placebo, and 53 per cent of those who had received the antihistaminic drug thought that the medication had helped their symptoms. The rate of cure of any symptom was about the same in both groups, except that cough seemed to disappear more quickly when the antihistaminic was given. There was also no detectable difference in both groups when compared on the basis of duration of symptoms prior to the onset of therapy. Ten per cent of the patients who received the drug reported toxic reactions and 15 per cent who received the placebo had similar reactions. A similar study was made with another more potent antihistaminic agent. Similar results were obtained. It is suggested that any study based on a subjective appraisal of symptoms is of doubtful scientific value. Also, the common cold is a variable entity and many patients recover spontaneously from the initial symptoms. The beneficial effects of antihistaminic drugs in the treatment of the common cold appeared to be questionable. B. S.

Antihistaminic Drugs: Comparative Activity in Man as Measured by Histamine Iontophoresis. Sternberg, T. H., Perry, D. J., and LeVan, P.: J. A. M. A. **142**: 969, 1950.

The antihistaminic activity of thirteen commercially available drugs was measured in human beings by determining their effect upon the threshold of the whealing response of the skin to serial dilutions of histamine introduced iontophoretically. When the initial threshold had been established, the test drug was administered orally and the threshold was again determined one or two hours later, at which time the activity of the drug was maximal. The difference between the two readings was regarded as a measure of the antihistaminic activity of the drug. The results indicated that Pyribenzamine, Neoantergan, and Benadryl are the most effective antihistaminic agents. A wide variation in the activity of the same drug was noted in different individuals. F.

Eosinopenia Due to Glucose Administration. Jordan, P. H., Last, J. H., Pitesky, I., and Bond, E.: Proc. Soc. Exper. Biol. & Med. **73**: 243, 1950.

Hyperglycemia was produced by oral or intravenous administration of glucose in trained unanesthetized dogs. Repeated absolute eosinophile counts showed an eosinopenia when compared with counts obtained in a control experiment on the same dog. The maximum eosinopenic response occurred at about four hours which is in keeping with the response following the administration of epinephrine, ACTH, or C_{11} steroids. The authors believe that hyperglycemia may initiate the release of insulin which may directly stimulate the release of ACTH from the pituitary gland. I. GLAZER.

Effect of Antihistaminic Drugs on the Sensibility of the Skeletal Muscle to Acetylcholine and Potassium. Glanzmann, S., and Salva, J. A.: Acta allergologica **2**: 277, 1949.

The modifying effect of various antihistaminic drugs on the contraction of frog's skeletal muscle produced by acetylcholine and potassium was studied. Benadryl, Antistine, Neoantergan, Pyribenzamine, and Phenergan reduced the response to both acetylcholine and potassium. The parallel qualitative and quantitative effects of the five antihistaminics studied suggested that they act directly on striated muscle. H.

Inhibition of the Shwartzman Phenomenon by Adrenocorticotropic Hormone (ACTH) From the Adenohypophysis. Soffer, L. J., Shwartzman, G., Schneierson, S. S., and Gabrilove, J. L.: Science **111**: 303, 1950.

The Shwartzman phenomenon was elicited in twenty-six of twenty-eight rabbits with a meningococcus filtrate. When a sufficient dose of ACTH was administered prior to the provocative intravenous injection, the phenomenon was suppressed in eight of ten animals. When ACTH was given prior to the preparatory intracutaneous injection, there was no suppression of the phenomenon. The administration of surgical Pituitrin prior to the provocative injection failed to inhibit the Shwartzman phenomenon. Therefore, it appeared that the oxytoxic and pressor substances present in adrenocorticotropic hormone could not be responsible for the suppression of the reaction. It is suggested that this method may afford a new experimental approach for the elucidation of the beneficial therapeutic effect of ACTH in various collagen and vascular diseases. It might also be employed as a method for bioassaying the hormone. B. S.

Reduction in the Number of Circulating Eosinophils Following Induced Anoxemia. Penneys, R., Thomas, C. B., and Lewis, R. A.: Bull. Johns Hopkins Hosp. **86**: 102, 1950.

A gas of low oxygen concentration was administered to eleven healthy subjects so that their arterial oxygen saturation was lowered to between 80 and 70 per cent for from seventeen to twenty-four minutes. There was a mean reduction of 40 per cent in the circulating eosinophil counts taken four and one-half hours after the test and one-half hour before the test. The control eosinophil counts taken when the subjects were not exposed to anoxia fluctuated in both directions with a mean change of 0 per cent. The authors believe that there was an increase in adrenal cortical activity following anoxemia. I. GLAZER.

Role of Sludged Blood in Allergy: Use of Heparin. Timoneu, S., and Zilliacus, H.: Acta. med. Scandinav. **135**: 292, 1949.

Intravascular aggregation of red cells, sludged blood, was noted in twelve patients being treated for various allergic skin conditions. The administration of heparin intravenously, four times daily, was effective in decreasing the red blood cell aggregations and increasing the rate of blood flow. Antihistaminic drugs also reduced the cellular aggregation, but were less effective than heparin. Treatment with either heparin or antihistaminic drugs resulted in improvement of the allergic symptoms. It is believed that the aggregation phenomenon represents either an antigen-antibody reaction or an "alarm reaction" and that heparin prevents the release of histamine from the red blood cells into the plasma. H.

Reactions of the Isolated Surviving Coronary Artery to Epinephrine, Acetylcholine and Histamine. Smith, D. J.: Proc. Soc. Exper. Biol. & Med. **73**: 449, 1950.

Angioplethysmokymography was used to study volume changes of perfused isolated surviving blood vessels. Acetylcholine or histamine, when added to the perfusate in varying doses, uniformly produced vasoconstriction of coronary arteries of man, pig, and sheep. The effect of epinephrine depended on the degree of vasomotor activity of the segment under test; those coronaries which were nearly completely dilated responded by a slight and transient vasoconstriction, while those which were not so completely dilated always responded to epinephrine by dilatation. I. GLAZER.

Release of Histamine During Hemolytic Reactions in the Blood of Rabbits. Carryer, H. M., and Code, C. F.: Proc. Soc. Exper. Biol. & Med. **73**: 452, 1950.

Either a suspension of washed sheep red cells or physiologic saline was added to the heparinized blood of rabbits sensitized to sheep erythrocytes. After incubation for one hour at 37° C. and centrifugation, the supernatant fluid was found to contain from two to fifteen times as much histamine as the controls. The histamine was not derived from the hemolysed sheep red cells, since they contain very little histamine. In all likelihood, it was released from the formed elements of the rabbit blood during the hemolytic reaction. I. GLAZER.

Histamine Metabolism in Pregnancy. Kapeller-Adler, R.: Lancet **257**, 745, 1949.

Using a biologic technique, the histamine content of the plasma and the blood cells was estimated separately in various stages and conditions of pregnancy. The histaminase activity of these sera was simultaneously determined by a colorimetric method. In eight nonpregnant women, histaminase could not be detected in the serum and only traces of histamine were found in the plasma of four of these individuals. In twenty-five cases of normal pregnancy, high serum histaminase levels were obtained, with the peak levels occurring between the seventh and eighth months. The concentration of histamine in the plasma and blood cells of these patients was about the same as that in the nonpregnant group. Sixteen cases of mild toxemia of pregnancy showed serum histaminase and blood cell histamine levels which did not differ greatly from those in normal pregnancy. The plasma histamine levels were much higher in this group. In sixteen cases of moderate or severe toxemia, the histaminase and blood cell histamine concentrations diminished appreciably, while the plasma histamine levels became distinctly elevated. During labor, there was a drop in the serum histaminase and blood cell histamine levels and a rise in the plasma histamine concentration. Four of five cases of pyelitis of pregnancy showed a rise in the plasma histamine level with no change in the serum histaminase activity. Three of four cases of threatened abortion showed considerable amounts of histamine in the plasma, but little histaminase activity.

It is suggested that the histamine metabolism in pregnant women differs from that in nonpregnant women. In pregnancy, histamine can easily shift from the cells into the tissue fluids. This hypothesis seems to be substantiated by the increase in serum histaminase observed throughout normal pregnancy which apparently acts as a protective mechanism. In severe cases of toxemia, a decreased serum histaminase activity always seems to be associated with a low histamine content of the blood cells and a high plasma histamine. In these

cases, it is possible that the histamine, not metabolized by histaminase, is extravasated into the surrounding tissue where it exerts its toxic effects. It is also suggested that the high plasma content of histamine during parturition and threatened abortion may indicate that histamine plays a role in these conditions. Since it is generally accepted that histaminase is produced in the placenta, any degenerative changes in this structure may be responsible for diminished activity of the serum histaminase in pregnancy. B. S.

Miscellaneous

Antihistaminic Drugs for Colds. Evaluation Based on a Controlled Study. Hoagland, R. J., Deitz, E. N., Myers, P. W., and Cosand, H. C.: J. A. M. A. **143**: 157, 1950.

The antihistaminics, Pyribenzamine and Tagathan, and a placebo were administered by the oral and intranasal routes to a selected group of 190 soldiers suffering from head colds. Treatment was begun either early or late in the course of the cold. Twenty-seven per cent of the patients who received the placebo and a comparable percentage of those who received the antihistaminics reported cures within twenty-four hours. The time of the administration of the drugs failed to influence the percentage of cures. There was, however, a definite decrease of the serous nasal discharge among the patients receiving the antihistaminics. This finding was not observed in the controls. The results of treatment by the oral and nasal routes were essentially the same. F.

Serological Reactions in Rheumatoid Arthritis. I. Factors Affecting the Agglutination of Sensitized Sheep Erythrocytes in Rheumatoid-Arthritis Serum. Pike, R. M., Sulkin, S. E., and Coggeshall, H. C.: J. Immunol. **63**: 441, 1949.

Serum from patients with rheumatoid arthritis increased both the agglutination and hemolysis of sensitized sheep cells. The effect upon the agglutination reaction was demonstrated more consistently than the effect upon the hemolysis reaction. The agglutination-producing factor remained active after storage of the arthritis serum for several months. R. Wiseman.

Effectiveness of Various Drugs in Prevention of Airsickness. Chinn, H. I., and Oberst, F. W.: Proc. Soc. Exper. Biol. & Med. **73**: 218, 1950.

Dramamine is the 8-chlorotheophylline salt of β-dimethylaminoethyl benzhydryl ether (Benadryl). The effectiveness of Dramamine and of either of its components, Benadryl or 8-chlorotheophylline, in the prevention of airsickness was tested with a simulated turbulance technique in an airplane. There was no significant difference between the effectiveness of Benadryl (50 mg.) and Dramamine (100 mg.). Slight protection was afforded by 8-chlorotheophylline (50 mg.). A combination of hyoscine hydrobromide (0.65 mg.) and Benadryl (50 mg.) was more effective than either drug alone. I. Glazer.

Fluorescent Development of Adrenaline in Paper Chromatograms. Shea, S. M.: Nature **165**: 729, 1950.

In alkaline solution, adrenaline forms leucoadrenochrome which produces an apple-green fluorescence when exposed to ultraviolet light. Using liquefied phenol as a solvent, the position of adrenaline on a paper chromatogram could be determined by exposing the strip to ultraviolet light in a vapor of concentrated ammonia. I. Glazer.

Production of Antisera in Rabbits Using Calcium Alginate as an Antigen Depot. Slavin, D.: Nature **165**: 115, 1950.

The alginates are salts of alginic acid derived from seaweed. The sodium salt is a viscous fluid which, on the addition of calcium chloride, is changed immediately into a calcium gel. In order to prepare antibacterial sera, rabbits were injected intraperitoneally with a concentrate of dead broth cultures emulsified in a 5 per cent sodium alginate solution (pH 7.2). Immediately, thereafter, 1 per cent aqueous calcium chloride was inoculated into the same site. Three or four weeks later, the same antigen was injected intravenously. Ten days after the intravenous injection, the blood sera had agglutinin and precipitin titers as good as, or better than, those obtainable by any other method. Rabbits killed six weeks after the alginate inoculation still had, in their peritoneal cavities, encapsulated collections of alginate which were intersected with trabeculae rich in reticuloendothelial cells. This method of antibody production is safer for the animal than the intermittent intravenous injections of graded doses and involves less work. I. GLAZER.

Precipitin Production in Chickens. V. The Effect of Splenectomy on Antibody Formation. Wolfe, H. R., Norton, S., Springer, E., Goodman, M., and Herrick, C. A.: J. Immunol. **64**: 179, 1950.

Nine splenectomized and eight normal chickens were given single intravenous injections of beef albumin. Antibody nitrogen titrations seven days later showed high titers in the control series, but practically no response in the splenectomized animals. A single intravenous injection of minute quantities of antigen in normal chickens produced antibodies, while large amounts of beef albumin did not stimulate antibody formation in the splenectomized animals. When splenectomized chickens received two series of injections over a period of several weeks, uniformly high antibody titers were obtained. Hence, splenectomized fowls were capable of antibody formation, but required intense antigenic stimulation to do so. In this species, the spleen appears to play an active role in antibody production. R. WISEMAN.

Procedure for Determination of Aerosol Delivery and Stability During Nebulization. Abramson, H. A., Sklarofsky, A. B., and Recter, C.: Ann. Allergy **7**: 612, 1949.

Aerosol particles smaller than 3 micra cannot be trapped by liquids at room temperatures. A centrifugal coil for aerosol collection is described and the action of the De Vilbiss No. 40 nebulizer under varied conditions was studied. Phenolsulfonphthalein and sodium ascorbate were employed as test solutions. It was found that, under constant conditions, delivery rose from 4.3 per cent at 4.5 liters of airflow per minute to 43.3 per cent at 11.5 liters per minute. With constant velocity of airflow, increasing the phenolsulfonphthalein concentration from 4.2 mg. to 35.6 mg. failed to influence the percentage delivered. However, the total P.S.P. delivered by the nebulizer increased from 0.6 mg. with 4.2 mg. per c.c. initially to 5.2 mg. delivery with 3.6 mg. per c.c. initially. The milligrams of P.S.P. delivered per liter per minute likewise rose from 0.016 to 0.124 mg. per liter per minute. The addition of glycerol did not influence the percentage of delivery but at a glycerol concentration of 25 per cent the coefficient of viscosity was doubled. Aerosol experiments with sodium ascorbate indicated that aerosolization time might be shortened and mucous membrane irritation diminished by increasing the airflow time to 10 liters per minute, by increasing the concentration of the medication, or by using nasal tips. W.